Karolinska Institutet

Institutionen för Mikrobiologi, Tumör och Cellbiologi

Rift Valley fever virus - vaccine strategies

AKADEMISK AVHANDLING
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ABSTRACT

Rift Valley fever virus circulates throughout Africa and the Arabian Peninsula and is of great concern for animal and public health. Infections in humans are often manifested as mild self-limiting illness, although in some cases there are more severe symptoms such as neurological complications and hemorrhagic fever. Spontaneous abortions among livestock are a hallmark for Rift Valley fever virus outbreaks and disease in small ruminants often has a deadly outcome. At present, there is no vaccine available for use in humans and the ones used in livestock are either poorly immunogenic or cause severe adverse effects. The economic impact of this pathogen in the form of livestock losses and restrictions on the trade of animals and animal products as well as its significance in relation to public health underscores the importance of developing safe and effective vaccines. The main focus of this thesis was to evaluate existing vaccines and novel vaccine candidates, with special emphasis on vaccine platforms practical in resource-poor areas.

It is difficult to maintain a cold-chain during transit in Mozambique and the inactivated Rift Valley fever virus vaccine is transported more than 2000 km within the country before it is administered to livestock in Zambezia Province. For that reason, the vaccine was evaluated for its ability to induce antibodies in cattle after storage at ambient temperatures. Importantly, the storage and transport conditions used in Mozambique did not have an adverse effect on the antibody responses induced by the vaccine. When performing the aforementioned study, we found evidence of previous Rift Valley fever virus infections in livestock in Maputo Province, a region where there had been no recorded evidence of the virus since 1969. A cross-sectional seroprevalence study was undertaken to examine the need to implement a vaccination program in this particular province. Unexpectedly, seroconversion was observed in 37% of the investigated cattle, suggesting that this pathogen is widely distributed throughout Maputo Province.

Rift Valley fever virus is highly pathogenic and to circumvent the handling of replicating virus during the vaccine manufacturing process would be advantageous. Other highly desirable vaccine-characteristics are low production costs, high immunogenicity to reduce the number of doses, and a non-invasive delivery route to avoid the challenge of maintaining sterility of hypodermic equipment. To fulfill some of those requirements we developed and evaluated three different vaccine strategies *i)* DNA vaccines, *ii)* vaccine based on virus-like particles, and *iii)* plant-derived protein subunit vaccines. All candidates induced vaccine-specific antibody responses in mice and the DNA- and virus-like particle-based vaccines conferred protection against Rift Valley fever disease.

Here, we raise the question of extending the vaccination program in Mozambique to include Maputo Province. We show that the inactivated virus vaccine is well-suited for that purpose until more effective alternatives are available. In the search for such an alternative, we evaluated three vaccine candidates. One of those candidates, vaccine based on virus-like particles, was found to have good prospects as a future Rift Valley fever virus vaccine.

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